REMARKS

Prior to the present First Amendment and Response to Non-Final Office Action ("Response"), Claims 1-72 were pending. In this Response, applicants cancel Claims 3 and 25-72, amend Claims 1, 2, 8, 12, 13, 14, 19, 21 and 24, and add new Claims 73-75. The claim amendments and new claims do not introduce any new matter. Claims 1-2, 4-24 and 73-75 will be pending after entry of the amendments.

Restriction/Election

Applicants cancel Claims 25-72 as non-elected.

Support for Claim Amendments and New Claims

Support for amendments to Claims 1, 2, 8, 12, 13, 14, 19, 21 and 24 and new Claim 73 is found throughout the specification, for example, in Example 2, from p. 38, line 23, through p. 39, line 6. New Claim 75 is based on Claim 1. Further support for new Claim 75 and also for new Claim 74 is found, for example, on p. 2, line 28, and on p. 19, line 8.

Rejection of Claims under 35 U.S.C. § 112, Second Paragraph

The Examiner rejects Claims 1-24 under 35 U.S.C. § 112, second paragraph, as indefinite. The Examiner asserts that the phrase "substantially modify" "in claim" [*sic*] is not clearly defined, and that applicants have not defined or explained clearly the extent of substantial modification of the low density lipoprotein. Applicants assume that the Examiner refers to Claim 1, which recites the term "substantially modify" within the limitation "wherein the exposure [to a lipid removing agent] does not substantially modify the low density lipoprotein...".

Applicants respectfully assert that the specification provides at least one criterion for determining when the exposure to a lipid removing agent does not substantially modify the low density lipoprotein particles. The specification teaches, in Examples 2, 3 and

5: "this delipidation method created HDL particles associated with Apo A-1 that were low or substantially devoid of cholesterol and phospholipid ... Lipid was only slightly removed from LDL particles (Apo B) with this method ..." (see p. 38, line 6, through p. 39, line 3); "[t]his method reduced total cholesterol by 9% and phospholipids by 9%. A decrease of about 14% was observed in Apo A-1. ... There was little effect on Apo B associated LDL particles... (see, respectively, p. 39, lines 20-26); "the Apo B associated with LDL ... remains substantially unchanged" (and p. 40, line 15). Based on the explanations provided in the specification, the phrase "does not substantially modify" recited in Claim 1 is clear, the degree of modification is assessed in reference to the lipid content of the low density lipoprotein. Accordingly, applicants respectfully request withdrawal of the rejection of Claims 1-24 as it relates to the phrase "substantially modify" recited in Claim 1.

The Examiner also objects to the phrase "substantially similar" in Claim 3. The Examiner asserts that this term is not defined in the claims or in the specification. Applicants cancel Claim 3, thereby rendering the rejection of this claim moot.

In view of the foregoing, applicants respectfully request that the rejection of Claims 1-24 under 35 U.S.C. § 112, second paragraph, be withdrawn.

Rejections of Claims under 35 U.S.C. § 102(b)

Rejections of Claims 1-24 under 35 U.S.C. § 102(b) as anticipated by Dass

The Examiner rejects Claims 1-24 under 35 U.S.C. § 102(b) as anticipated by Dass, C.R., and W. Jessup, *Drug Delivery*, 2000, Vol. 7 (3): 161-182 (hereinafter "Dass"). Applicants respectfully traverse the rejection.

The Examiner asserts that, in Table 1 on p. 167, Dass teaches all the elements of Claims 1-24. Applicants disagree. Applicants respectfully bring to the Examiner's attention that Dass is a review article. Table 1 on p. 167 discloses 11 types of HDL particles from different original articles. Table 1 in Dass is silent as to the origin of the presented

HDL particles, and fails to teach how their lipid or cholesterol content is different from that of the naturally occurring high density lipoprotein particles. Upon amendment, Claim 1 recites obtaining a mixture of the high density lipoprotein particles and low density lipoprotein particles from a biological fluid. Claim 1 also recites a particle derivative [of at least one form of high density lipoprotein particle] that has a lower content of at least one of lipid or cholesterol than the high density lipoprotein particles prior to exposure to the lipid removing agent. Applicants respectfully assert that Dass fails to teach the particle derivative recited in Claim 1, and fails to anticipate Claims 1-2 and 4-24. Claim 3 is cancelled, thereby rendering its rejection moot. Applicants respectfully request withdrawal of the rejection of Claims 1-2 and 4-24 under 35 U.S.C. § 102(b) as anticipated by Dass.

Rejections of Claims 1-24 under 35 U.S.C. § 102(b) as anticipated by Tricerri

The Examiner rejects Claims 1-24 under 35 U.S.C. § 102(b) as anticipated by Tricerri *et al.*, *J. Lipid Res.* 2002 Vol. 43 (2) 187-97 (hereinafter "Tricerri"). Applicants respectfully traverse the rejection.

The Examiner asserts that Tricerri teaches all elements of Claims 1-24. Applicants respectfully disagree. Tricerri examines the ability of the conformations of ApoA-1 in reconstituted HDL particles to bind to and abstract lipids from unilamellar vesicles. Tricerri asserts that the study provides a model system for studies of cholesterol transport. Tricerri teaches two types of discoidal, reconstituted HDL particles consisting of only purified human ApoA-I (two molecules ApoA-I per particle), phospholipid (phosphatidylcholine) and sodium cholate.

In contrast, amended Claim 1 recites a particle derivative of at least one form of high density lipoprotein particle formed by obtaining a mixture of the high density lipoprotein particles and low density lipoprotein particles from a biological fluid and exposing the mixture to a lipid removing agent. The particle derivative has a lower content of at least one of lipid or cholesterol than the high density lipoprotein particles prior to exposure to the lipid removing agent.

In contrast to the reconstituted particles disclosed in Tricerri, the particle derivatives recited in Claim 1 are obtained from the high density lipoprotein particles naturally occurring in a biological fluid, such as plasma. Accordingly, the properties of the particle derivatives, as recited in Claim 1, are inherently different from those of the reconstituted particles in Tricerri. For example, unlike the reconstituted particles in Tricerri, which consist of only human apolipoprotein A-1, phospholipid (phosphatidylcholine) and sodium cholate, applicants' naturally-based particle derivatives inherently comprise other components found in natural high density lipoprotein particles, such as apolipoprotein A-2. Tricerri fails to teach the naturally derived particles that inherently comprise other components, such as apolipoprotein A-2. For at least this reason, Tricerri fails to anticipate the pending claims. In view of the foregoing, applicants respectfully request withdrawal of the rejection of Claims 1-2 and 4-24 under 35 U.S.C. § 102(b) as anticipated by Tricerri. Claim 3 is cancelled, thereby rendering its rejection moot.

Rejections of Claims 1-24 under 35 U.S.C. § 102(b) as anticipated by Ito

The Examiner rejects Claims 1-24 under 35 U.S.C. § 102(b) as anticipated by Ito *et al., J. Lipid Res.* 2000 Vol. 41 (6) 894-904 (hereinafter "Ito"). Applicants respectfully traverse the rejection.

The Examiner asserts that Ito teaches all elements of Claims 1-24. Applicants respectfully disagree. Ito examines the effect of the digestion of cellular sphingomyelin on the apolipoprotein-mediated release of cholesterol and phospholipids from rat cells. Ito discloses particles consisting of only purified human apolipoprotein A-1, cholesterol, and rat phospholipids. The particles in Ito are obtained by incubating apolipoprotein A-1 with rat astrocytes and meningeal fibroblasts.

In contrast, Claim 1, upon amendment, recites a particle derivative of at least one form of high density lipoprotein particle formed by obtaining a mixture of the high density lipoprotein particles and low density lipoprotein particles from a biological fluid and exposing the mixture to a lipid removing agent. The resulting particle derivative has a lower

content of at least one of lipid or cholesterol than the lipid or cholesterol content of the high density lipoprotein particles prior to exposure to the lipid removing agent.

Applicants' claimed particle derivatives are obtained from the high density lipoprotein particles naturally occurring in a biological fluid, such as plasma. Accordingly, the properties of the particle derivatives are inherently different from the reconstituted model particles in Ito. For example, unlike the reconstituted particles in Ito, applicants' naturally-based particle derivatives inherently comprise other components found in natural high density lipoprotein particles, such as apolipoprotein A-2. Ito fails to teach applicants' claimed particles which are derived from high density lipoprotein particles naturally occurring in a biological fluid that inherently comprise other components, such as apolipoprotein A-2. Accordingly, for at least this reason, Ito fails to anticipate the claims of the present application, as amended. In view of the foregoing, applicants respectfully request withdrawal of the rejection of Claims 1-2 and 4-24 under 35 U.S.C. § 102(b) as anticipated by Ito. Claim 3 is cancelled, rendering its rejection moot.

CONCLUSION

The foregoing is submitted as a full and complete response to the Non-Final Office Action mailed January 26, 2005. No additional fees are believed due, however, the Commissioner is hereby authorized to charge any deficiencies which may be required or credit any overpayment to Deposit Account Number 11-0855.

Applicants assert that the claims are in condition for allowance and respectfully request that the application be passed to issuance. If the Examiner believes that any informalities remain in the case that may be corrected by Examiner's amendment, or that there are any other issues which can be resolved by a telephone interview, a telephone call to the undersigned agent at (404) 815-6102 or to Dr. John McDonald at (404) 745-2470 is respectfully solicited.

Respectfully submitted,

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